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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/902,572	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/19/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 September 2005 has been entered.

Claims 39-43 were previously considered. Claim 39 was amended in the 19 September Paper. Claims 39-43 are pending and under consideration.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 101 and 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 39-43 **stand rejected** under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for reasons of record and herein below. The *prima facie* rejection was made in the Office Action mailed 26 February 2003 and is reiterated herein.

Each of the claims is directed towards an antibody that binds to the polypeptide described by SEQ ID NO: 255. The antibody can be a fragment that binds to SEQ ID NO: 255. The

antibody can be a monoclonal antibody. The antibody can be labeled. The antibody can be humanized. The antibody can "specifically" bind to the polypeptide shown in SEQ ID NO: 255. Any utility for the claimed antibodies must be specific and substantial, or well established, for the protein encoded by SEQ ID NO: 255. Utilities simply directed to detection of, or purification of, the protein described by SEQ ID NO: 255 cannot be considered as substantial (i.e. having a "real-world" use) in the absence of a specific and substantial, or well-established utility for the protein to which the antibody binds. No such specific and substantial or well-established utility has been described for the protein described by SEQ ID NO: 255.

SEQ ID NO: 255 appears to have been novel in the art at the time of filing. Likewise, the nucleic acid sequence disclosed by applicants as encoding SEQ ID NO: 255, SEQ ID NO: 254, appears to be novel in the art. Therefore, there is no well-established utility for the disclosed protein or antibodies specific for the protein.

The specification asserts that, based upon BLAST and FastA sequence analysis, various portions of PRO302 have significant homology with various protease proteins (page 110, top paragraph). Exactly which portions have homology to which portions of which other known proteases is not taught, however. Based upon the assertion that PRO302 comprises proteolytic activity, the specification asserts that PRO302 has utility in vivo for therapy as well as in vitro utilities. There is no indication in the specification that the supposed protease has any *specific* target for its supposed activity (e.g. association with a particular disease or specific substrate). There is no specific disease or condition shown in the prior art or instant specification to be associated with the protein described by SEQ ID NO: 255.

It is not likely that one of skill in the art could reasonably predict based upon the primary sequence of SEQ ID NO: 255 what specific activity PRO302 may have. The relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that "Thus, one of the "grand challenges" of high-performance computer-predicting the structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning protein structure, and failures to make it predictable. Thus, as taught by Berendsen, it is unlikely that one could predict the structural/functional characteristics of PRO302 based upon primary sequence alone. Further supporting Berendsen's teachings, Galparin et al (Nature Biotechnology, Vol. 18, pages 609-613, June 2000; see the entire reference) teach that "sequence comparison methods, even the best ones, are of little help when a protein has no homologs in current databases or when all database hits are to uncharacterized gene products." Galperin et al disclose, "assessing the actual power of the context based method for protein function prediction requires extensive testing by labor-consuming, case-by-case, computational, and eventually experimental analysis." Attwood (Science, Vol. 290, pages 471-473, see the entire reference) also states that it is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences." It is clear from the cited references that one cannot reliably predict based upon primary structure alone or on mere sequence homology what specific activity PRO302 might possess.

The specification does teach in Example 85 that the PRO302 protein has an effect on vascular leakage when injected into hairless guinea pigs. While the specification concludes that PRO302 protein can induce vascular permeability in the guinea pig model, it does not give the actual data or an indication of the relative activity of the PRO302 protein compared to the positive control. In addition to not providing a basis for one of skill in the art to determine the actual effectiveness of PRO302 in inducing vascular permeability, the specification does not provide a basis to envision a specific, real-world application for the asserted ability to induce vascular permeability. Based on these teachings, one of skill in the art at the time of applicants' invention would not be able to recognize a specific utility (e.g. specific proteolytic substrate) or substantial utility (i.e. not requiring additional research in order to confirm a real-world application for the claimed proteins) for the claimed proteins. Because no specific and substantial or well-established utility has been demonstrated for the protein described by SEQ ID NO: 255, one of skill in the art would not have been able to recognize a specific and established utility for the claimed antibodies.

Claims 39-44 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Arguments

In response to the *prima facie* case and arguments of record, Applicant first summarizes the "Legal Standard for Utility under 35 U.S.C. §101", which summary is acknowledged to be accurate.

It is noted, however, that the summary (page 6) quotes from MPEP §2107 II (B)(1) as follows, "If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose... and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility." The phrase omitted by Applicant reads as follows "(*i.e.*, it has a specific and substantial utility)". As repeatedly stated throughout prosecution of the instant application, the issue at hand is whether a "specific" and "substantial" utility has been asserted in the application or would be readily apparent to the skilled artisan based on the disclosure of the invention. The complete passage clearly indicates that a rejection should not be imposed only if the asserted utility is both "specific" and "substantial", which requirement is clearly stated in the paragraph that immediately follows the paragraph cited by Applicant.

Finally, the Utility Guidelines make clear, "[u]tilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities." MPEP 2107.01 I. B.

Applicant's subsequent arguments are directed to the showings of the Rule 1.132 Declaration filed with the 19 September Paper.

Declaration of Sherman Fong, Ph.D. under 37 CFR §1.132

Declarant first cites Miles *et al.*, which is submitted as Exhibit A as teaching the skin vascular permeability assay, disclosed in the instant application as Assay #64, and asserts that the assay has been reliably used for identifying proinflammatory molecules (Paragraph 6).

In Paragraph 7, Applicant states that proinflammatory molecules can directly or indirectly cause vascular permeability, which provides for extravasation of leukocytes at a site of infection or injury (illustrated in Exhibit B).

In paragraph 8, Declarant states that proinflammatory molecules are useful in treating infections, as local administration would stimulate and attract immune cells to the cite of infection. Declarant cites MIP-1 and MIP-2 as molecules that induce neutrophils to extravasate, CXC chemokines as activators of neutrophils and non-CXC chemokines as chemotactic agents for T lymphocytes. Declarant further states that inappropriate expression of proinflammatory molecules may cause an abnormal immune cell response and leading to tissue destruction and cites various examples of abnormal immune cell responses. Still further, Declarant states that proinflammatory molecules with angiostatic properties are useful in inhibition of angiogenesis in abnormal wound healing, abnormal inflammation or abnormal neovascularization.

In paragraph 9, Declarant states that Miles *et al.* (Exhibit A) used the skin vascular permeability assay to identify proinflammatory and immune related molecules.

In paragraph 10, Declarant states that the skin vascular permeability assay was used in the clinic in determining if factor XIII could be used to treat an immunovascular disease by determining if factor XIII could inhibit vascular permeability induced by anti-endothelial cell antibodies.

In paragraph 11, Declarant states that the skin vascular permeability assay was used to identify VPF (VEGF).

In paragraph 13, Declarant states that the skin vascular permeability assay was performed using purified PRO polypeptide and cites Exhibit I as an example of positive results from a PRO polypeptide.

In paragraph 14, Declarant states the opinion that the PRO polypeptide that shows activity in the skin vascular permeability assay has specific and substantial utility. Declarant states, "examples of utilities include, enhancing immune cell recruitment to sites of injury or infection, or inhibitors to treat autoimmune diseases such as psoriasis *etc.* as discussed above. Furthermore, the angiogenic or angiostatic properties of proinflammatory molecules would also find practical utility in controlling tumorigenesis."

In the arguments beginning on page 6, Applicant submits that the skin vascular permeability assay (#64) discussed in the Declaration is the same as the vascular leakage assay (#51) for which PRO302 (the claimed polypeptide) was identified as positive except that Assay #64 is followed up with a biopsy. Applicant contends that when one measures vascular "Permeability" versus "Leak" with these assays, one is measuring exactly the same proinflammatory activity. Applicant submits, based on the positive results of the vascular leak assay, "Inhibitors of the PRO302 molecule, like anti-PRO302 antibodies, are useful in treating conditions with abnormal immune cell responses like autoimmune diseases, psoriasis, etc., as discussed in the Fong declaration and are art accepted utilities for proinflammatory molecules. Hence, one skilled in the art would readily understand and accept as substantial, credible and

specific, utilities at the effective filing date of the present application, based on a positive score in the "vascular permeability Assay-assay#51).[sic]"

The showings of the Declaration and Applicant's arguments have been fully considered but are not deemed persuasive. It is first noted that the Declaration does not contain any data specific to the PRO302 polypeptide (*i.e.*, the target for the claimed antibody). Instead, the declaration refers to, and presents data from an unidentified "PRO polypeptide". Furthermore, it is noted that the biopsy in Assay #64 "is evaluated for inflammatory cell infiltration into the skin. Sites with visible inflammatory cell inflammation are scored as positive. Inflammatory cells may be neutrophilic, eosinophilic, monocytic or lymphocytic. At least minimal perivascular infiltrate at the injection site is scored as positive, no infiltrate at the site of injection is scored as negative" (specification, page 210, lines 34-37). Still further, it is noted that PRO302 is not listed among the polypeptides scored as positive in the skin vascular permeability assay (bridging pages 210-211).

In contrast to Assay #64, Assay #51 does not involve assessment of the injection sites for immune cell infiltrates, which would seem critical to determining whether the polypeptide is a proinflammatory molecule. This is evidenced by the stated purpose of each assay. The specification states, "[t]his assay [Assay 51] is designed to determine whether PRO polypeptides of the present invention show the ability to induce vascular permeability" (page 215, lines 30-31) and "[t]his assay [Assay 64] shows that certain polypeptides of the invention stimulate an immune response and induce inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal" (page 210, lines 23-24). Clearly, if the only

difference between the assays is the biopsy, then the biopsy is critical to determining stimulation of an immune response and induction of inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection. Additional evidence that a positive result in Assay #51 does not establish that a molecule has proinflammatory activity is that VEGF is used as a positive control in the assay. VEGF is not known in the art as a proinflammatory molecule (See *e.g.*, Swiss-Prot entry P15692; especially the "FUNCTION" section under the "Comments" heading).

Viewed as a whole, it is clear that a positive result in the Assay #51 indicates that a molecule might or might not have proinflammatory activity and the biopsy in Assay #64 is used to distinguish between these possibilities. The skilled artisan would view the fact that PRO302 is not listed among the polypeptides that were positive in Assay #64 as indicating either that PRO302 was tested and determined to be negative or that PRO302 was not tested in Assay #64. If the former is the case, clearly applicant's assertion that the claimed invention can be used to treat inflammatory diseases is groundless. If the latter is the case, then additional experimentation is required to reasonably establish that PRO302 has proinflammatory activity and that the claimed antibody has the utilities asserted by Applicant and Declarant.

It is further noted that, even if the declaration had included data demonstrating that PRO302 has proinflammatory activity, Applicant cannot rely on data that was not available to the skilled artisan at the time of filing to support a well-established utility.

> "If an application fails to disclose one specific, substantial, and credible utility, and the examiner discerns no well-established utility, the examiner will reject the claim under section 101.The rejection shifts the burden to the applicant to show that the examiner erred, or that a well-established utility would have been readily apparent to one of skill in the art. The applicant cannot rebut the rejection by relying on a utility that would not have been readily apparent at the time the application was filed. See, e.g., In re Wright, 999 F.2d 1557, 1562–63,

> 27USPQ2d 1510, 1514 (Fed. Cir. 1993)('developments occurring after the filing date of an application are of no significance regarding what one skilled in the art believed as of the filing date')." MPEP Federal Register / Vol. 66, No. 4 / Friday, January 5, 2001 / Notices at page 1095, bridging columns 1-2.

Next, Applicant submits that the art available at the time of filing show that the knowledge for vascular permeability factors was well correlated with diseases where "vascular leakage" is an issue. Applicant cites Dvorak as disclosing a vascular permeability factor (now known as VEGF) secreted by hepatocarcinoma cells, which was asserted to be useful for treating tumors. Applicant cites Connolly as showing that the same vascular permeability factor could stimulate endothelial cell growth and Olander as teaching methods of producing antibodies against Dvorak's VPF. Applicant contends that "a positive result in a Miles assay was considered adequate since **the art as a whole disclosed readily apparent utilities for vascular permeability factors in diseases** which included, but were not limited to, angiogenesis, wound healing, burns, antibodies to treat tumor growth, endothelial cells growth *etc.*" (first paragraph on page 8; emphasis in original).

Applicant submits that PRO302's utility lies in its use as a target for the development of anti-vascular leakage agents and urges, "[b]ased on the 'well-established' utilities for vascular permeability factors in the art as a whole, one skilled in the art would know how to use PRO302 (polypeptides and nucleic acids thereof), or anti-PRO302 antagonists (antibodies) to stop vascular leakage in a variety of disease conditions such as, pulmonary leakage, capillary leakage, tumor leakage, or in burns" (paragraph bridging pages 8-9). Applicant cites *Fujikawa v. Wattanasin* (CA FC) 39 USPQ2d 1895 (8/28/1996) and contends that a rigorous correlation need not be shown in order to establish a practical utility and that, based on positive results for

PRO302 in the well-established vascular permeability assay a nexus between PRO302 and "usefulness in disease" has been made.

These arguments have been fully considered but are not deemed persuasive. First, Applicant is reminded that each patent application must be examined on its own merits and the allowance of similar claims to others is immaterial to the allowability of the instant claims (see *In re Giolito*, 530 F.2d 397, 188 U.S.P.Q. 645 (C.C.P.A. 1976). The determination that the instant claims lack specific and substantial utility has been made based on the properties disclosed for the claimed invention in the instant specification, the art available at the time of filing and the Utility Guidelines published January 5, 2001 (*supra*).

Nevertheless, it is worth noting that the properties of the vascular permeability factor disclosed in the Dvorak *et al.*, Connolly *et al.* and Olander *et al.* patents is not limited to the ability of the exogenously added polypeptide to induce vascular permeability. In particular, Dvorak *et al.* establishes that the vascular permeability factor disclosed therein is secreted by tumors and antibodies raised against the vascular permeability factor were found to inhibit vascular permeability induced by tumor cells (see especially Examples 6, 7 and 10) and, as Applicant points out, Connolly teaches that the vascular permeability factor stimulates endothelial cell growth. Thus, the cited art does not support Applicant's contention that a positive result in the Miles assay alone was sufficient to support a well-established utility for a polypeptide.

In contrast to the teachings of Dvorak *et al.*, and as repeatedly pointed out by the Examiner in previous Office Actions, there is no evidence that the claimed PRO302 polypeptide has any role in naturally occurring pathology. Unlike the vascular permeability factor of Dvorak

et al. there is no evidence that the instant protein is secreted by tumors; therefore, the utility of the invention or reagents developed therewith to treat tumors would have to be established experimentally. Likewise, there is no evidence that the PRO302 polypeptide is in any way responsible for vascular leakage associated with pathological states such as tumors or burns such that the utility of anti-PRO302 antagonists to stop vascular leakage or the utility of PRO302 as a target for the development of anti-vascular leakage agents is established.

As stated in the Advisory Action mailed 16 March 2004, "[t]he skilled artisan would still have had to confirm that PRO302 plays some role in vascular physiology as part of its normal functions in the body in order to demonstrate a substantial utility for the protein in identifying antagonists of this particular activity. One cannot consider that developing antagonists to a protein that may only be involved in disrupting vascular integrity upon injection in large quantities under the skin, a completely artificial situation, as a 'real world' application in and of itself" (bridging pages 3-4). For example, it would not be surprising to find that the digestive enzyme trypsin disrupted vascular integrity upon injection in large quantities under the skin in view of its ability to disrupt basement membranes of adherent cells in culture. However, one would not expect that inhibitors of trypsin would have any therapeutic effect in treating tumors or burns because the enzyme is not present in tumors or burns.

With regard to the case law cited by Applicant, the question before the Court in *Fujikawa v. Wattanasin* was whether *in vitro* data presented for a claimed compound reasonably supported similar activity *in vivo*. The Court found, based on the facts in that case, that the *in vitro* data were reasonably correlative. In the opinion, the Court states, "each case of practical utility must be considered on its own facts" (at page 1899) and "there must be a sufficient correlation

between the tests and an asserted pharmacological activity so as to convince those skilled in the art, to a reasonable probability, that the novel compound will exhibit the asserted pharmacological behavior" (at page 1899). For reasons of record and herein above, in the instant case there is not sufficient correlation between the tests and an asserted pharmacological activity so as to convince those skilled in the art, to a reasonable probability, that the novel compound will exhibit the asserted pharmacological behavior.

Next, Applicant asserts that the absence of actual data showing the magnitude of the response to PRO302 is not relevant to the determination of whether the invention has a well-established utility. Applicant contends that it is sufficient that Applicant's have asserted that the measured difference was significant to establish that the molecule causes vascular leak and to identify therapies to stop vascular leakage.

This argument has been fully considered but is not deemed persuasive. Even if one were to accept, *arguendo*, that the disclosure is sufficient to establish that PRO302, when injected in large quantities under the skin, induces a significant degree of vascular leakage, the utility of the PRO302 polypeptide remains to be established. Throughout prosecution applicant has variously asserted that PRO302 is useful because it might play a role in pathologies associated with tumors or burns, might play a role in extravasation of T cells or might have proinflammatory properties useful in treating infections. However, given the disclosed properties of the PRO302 polypeptides, which amount to an assertion that various portions of PRO302 have significant homology with various protease proteins (page 110, top paragraph), although exactly which portions of which other known proteases is not taught, and a statement that PRO302 tested positive in a Guinea pig vascular leak assay (page 216, line 7), the skilled artisan simply would

not know which, if any, of these utilities are true. Therefore, no specific and substantial utility would be readily apparent to the skilled artisan based on the disclosed properties of the claimed invention.

Finally, Applicant contends that, the skilled artisan would appreciate, PRO302 antagonists, such as anti-PRO302 antibodies thereof are useful in treating diseases to stop vascular leak in a variety of diseases such as in angiogenesis, wound healing (pulmonary or capillary leakage), burns, tumor growth or leakage, etc. and that any experimentation that may occur towards this use is not undue since a specific, substantial and credible utility has been claimed for PRO302.

This argument has been fully considered but is not deemed persuasive because, for reasons of record and herein above, the skilled artisan would not recognize a specific and substantial credible utility for the claimed antibody. It is well established that the enablement requirement of § 112 incorporates the utility requirement of § 101.

> The how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112.

In re Ziegler, 992 F.2d 1197 (Fed. Cir. 1993; at 1200-01; citations omitted); see also *In re Kirk*, 376 F.2d 936 (C.C.P.A. 1967; at 942) ("Necessarily, compliance with § 112 requires a description of how to use presently useful inventions, otherwise an applicant would anomalously be required to teach how to use a useless invention."); *In re Brana*, 51 F.3d 1560, 1564 (Fed. Cir. 1995) ("Obviously, if a claimed invention does not have utility, the specification cannot enable one to use it."); Manual of Patent Examining Procedure § 2107.01. Thus, in light of the finding

that the application fails to satisfy the utility requirement under 35 U.S.C. §101, the application also fails to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph.

Applicant's arguments and the showings of the Declaration have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §101 and 112, first paragraph, as lacking a specific and substantial utility.

Claim Rejections - 35 USC § 112

Rejection of claims 39-43 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn**.

Applicant persuasively argues in the paragraph bridging pages 11-12 that the limitation "specifically binds" is a term of art, which would be understood by one of ordinary skill. It is further noted that essentially any protein will bind "non-specifically" to any other protein. Therefore, the skilled artisan would not have viewed the limitation as requiring that the claimed antibody bind only to PRO302 and no other proteins. With regard to the strength of binding required to meet the limitation, the limitation is reasonably construed as encompassing any saturable binding to the antigen which, although broad, is not indefinite.

New Grounds for Rejection

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 39 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 39, as written, does not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claim should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" if such limitation is supported in the application as filed. See MPEP 2105.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.
Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER